UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/951,188	10/15/1997	DAVID H. PRICE	IOWA-012/FUS	1309

23720 7590 05/18/2005

WILLIAMS, MORGAN & AMERSON, P.C.
10333 RICHMOND, SUITE 1100
HOUSTON, TX 77042

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/951,188	PRICE, DAVID H.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *See Continuation Sheet* is/are allowed.

6)☒ Claim(s) *137-143,149-151,157-161,163,164,167,168,177-180,203 and 218* is/are rejected.

7)☒ Claim(s) *144-146,162,169-172,174-176,204-207,217 and 220-226* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 110-113, 116-164, 167-172, 174-181, 184, 186-189, 191-193, 195-208, and 211-226 are pending in the application.

[2] Applicants' amendment to the claims, filed 2/1/2005, is acknowledged. This listing of the claims does not satisfy the requirements of the revised amendment practice according to 37 CFR 1.121 for reasons set forth in the "Notice of Non-Compliant Amendment" mailed 2/24/2005.

[3] Applicants' amendment to the claims, filed 3/11/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicants' arguments filed 2/1/2005 and 3/11/2005 are acknowledged. The arguments filed 2/1/2005 appear to be identical to the arguments filed 3/11/2005. Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Interview Summary

[6] Beginning at p. 28 of the response filed 3/11/2005 (the "Response"), applicants provide comments regarding telephonic interviews that were conducted during the months of July, August, and September 2004.

At the bottom of p. 28 of the Response, applicant's representative acknowledges agreement with the interview summaries and asserts that "certain points appear to have been overlooked." The first point is that "all pending claims except claims 133 and 136...were allowed by the Office" (emphasis in original) prior to the Office action mailed 3/19/2004. According to applicant, prior to allowance, the claims "had been drafted by, or under the express supervision of, Examiner Steadman and Brian Stanton."

The examiner acknowledges that certain claims were indicated in the Office action mailed 9/9/2003 as being in a condition for allowance and is reflected by the prosecution history. The Office action mailed 9/9/2003 was a final Office action. According to MPEP 706.07(d), "if ... the primary examiner finds the final rejection to have been premature, he or she should withdraw the finality of the rejection." Upon reconsideration of the claims, it was the examiner's position during the drafting of the Office action mailed 3/19/2004 that the specification does not enable the full scope of the claimed invention. The finality of the last Office action was withdrawn in favor of a non-final Office action mailed 3/19/2004. It is noted that, while certain claims were indicated as being in a condition for allowance in the Office action mailed 9/9/2003, the examiner knows of no requirement that once claims are indicated as being in a condition for allowance, the claims cannot be later rejected. To the contrary, MPEP 706.04 makes clear that claims held to be in a condition for allowance can be rejected if the "proposed rejection has been submitted to the primary examiner for consideration." In this case, (then junior) Examiner Steadman properly submitted the rejection to Primary Examiner Prouty for consideration as evidenced by Examiner Prouty's

signature on that Office action. Also, the MPEP does not direct the examiner to issue claims that do not meet the requirements of 35 U.S.C. 112, first and second paragraphs, 101, 102, and 103. In the Office action mailed 3/19/2004, the examiner set forth clear reasoning as to why the claims did not meet such requirements, particularly those claims rejected under 35 U.S.C. 112, first paragraph for scope of enablement. The line of reasoning for the rejection under 35 U.S.C. 112, first paragraph, and suggestions as to how to overcome the rejection were reiterated in each of the telephonic interviews held 7/27/2004, 8/3/2004, 8/10/2004, and 9/16/2004.

In response to applicant's representative's statement that prior to allowance, the claims "had been drafted by, or under the express supervision of, Examiner Steadman and Brian Stanton" is not correct. Prior to docketing this application to Examiner Steadman, this application has been under the "express supervision" of Examiners Lynette Smith and Peter Tung. The Office actions authored by Examiner Tung were signed by Examiner Prouty and Supervisory Examiner Achutamurthy. The application was then transferred to Examiner Steadman under the direction of Primary Examiner Prouty. During examination of the application, Examiner Steadman contacted Brian Stanton via e-mail to discuss proposed claims (claims 133-136 of the instant application), to which Mr. Stanton responded via email, providing suggested claim language. In this case, the application has been under the "express supervision" of examiners other than Examiner Steadman. Further, there is no indication in the prosecution history that the application has been under the "express supervision" of Brian Stanton.

Also addressing the first point, applicant states that during the interview it was indicated that in reinstating the scope of enablement rejection, the Office failed to meet its burden and that the reinstated scope of enablement rejection was inconsistent with the obviousness rejection. Applicant further asserts that during the interview, applicant stated the enablement rejection was improper because the cited page was not new evidence, was not pertinent to hybridization, and did not concern cyclins or cast doubt on the specification.

In response, it is noted that applicants were advised during the interview that, while the claims were previously indicated as being in a condition for allowance, the scope of enablement rejection was reinstated upon reconsideration and review of the specification. Also, it was noted that the scope of enablement rejection does not contradict the obviousness rejection. The examiner indicated that certain nucleic acids were enabled by the specification (see ¶ [12] at p. 6 of the previous Office action) and made an obviousness rejection (see ¶ [13] at p. 10 of the previous Office action) on the specific nucleic acids indicated as being enabled. The rejection under 35 U.S.C. 103(a) was not directed to those nucleic acids that were asserted to be non-enabled by the specification. As such, there is no inconsistency in the scope of enablement and obviousness rejections. Although applicants have raised this issue, that there is no inconsistency was expressed and made clear to applicant during the interview conducted 8/3/2004. Further, the examiner disagrees with applicants' assertion that the teachings of Branden et al. are not relevant to the scope of enablement rejection. The relevancy of the reference of Branden et al. was discussed in a previous Office action,

which is reiterated below. The examiner notes that applicants infer that the claimed nucleic acids encode only cyclins, however, the specification clearly states that "P-TEFb is a cyclin dependent kinase" (p. 204, line 15). Based on the teachings of the specification and the claims, it appears that P-TEFb is a dimer of two subunits – a cyclin moiety AND a cyclin-dependent kinase moiety.

Applicant's second point that is asserted to be missing from the interview summaries is an interview between Brian Stanton and applicant's representative on 8/11/2004, in which Mr. Stanton allegedly agreed that there were "gaps in reasoning" in the enablement rejection. According to applicant's representative, Mr. Stanton stated that, "O.K., we owe you a new office action." Applicants assert that although an agreement was reached, no "new" Office action was mailed.

In response, the examiner notes that MPEP 714.04 states, "[e]xaminers must complete an Interview Summary form PTOL-413 for each interview where a matter of substance has been discussed during the interview." However, it is noted that no Interview Summary form PTOL-413 exists for an interview conducted solely between Mr. Brian Stanton and applicants' representative on 8/11/2004. There is no dispute that such an interview took place. However, there is no written record by an examiner of such an interview, the examiner was never contacted by either Mr. Stanton or applicant's representative to discuss the telephonic interview of 8/11/2004, particularly the alleged "gaps in reasoning," and the examiner was never requested by Mr. Stanton or another representative of the USPTO to send a "new" Office action to restart the response period. The examiner was only apprised of the interview of 8/11/2004 by

applicant's representative during the telephonic interview of 9/16/2004. During the telephonic interview of 9/16/2004, it was agreed between the examiner and Ms. Reynolds that no new Office action would be mailed to applicant. It is noted that Mr. Stanton no longer holds a position of employment at the USPTO. Further, it is noted that during the three telephonic interviews conducted on 7/27/2004, 8/3/2004, and 8/10/2004, Mr. Stanton supported the examiner's position regarding the scope of enablement rejection under 35 U.S.C. 112, first paragraph. It is also noted that during the telephonic interview conducted on 9/16/2004, Ms. Reynolds also supported the examiner's position regarding the scope of enablement rejection and did not support the mailing of a new Office action as evidenced by the corresponding interview summary.

Applicant's third point is regarding written description support for claims 133 and 136. Applicant acknowledges that, even though the claims (prior to the instant amendment) recited the transitional phrase "comprising," the fragment was intended as being limited to the fragment of claim 113. Applicant notes that only claim 133 and not claim 136 was rejected for lack of written description.

The examiner acknowledges applicant's representative's comments. As applicant had yet to formally respond to the Office action mailed 3/19/2004 and in order to expedite prosecution of the application, it was noted during the telephonic interview conducted 7/27/2004 that claim 136 should have been rejected for lack of adequate written description.

Specification/Informalities

[7] The objection to the specification in the use of the trademarks "Centricon-30", "Mono S", and "Phenyl Sepharose" is maintained for the reasons of record (¶ [6] of the Office action mailed 3/19/2004). Applicant does not address this objection in the response filed 3/11/2005.

Claim Objections

[8] The objection to claims 208 and 211-216 (see ¶ [7] of the Office action mailed 3/19/2004) is withdrawn in view of the amendment to the claims.

[9] The objection to claims 140-143, 164, 167-172, 174-177, and 203-207 as being in improper form is maintained for the reasons of record (¶ [7] of the Office action mailed 3/19/2004).

[10] The objection to claim 151 (see ¶ [8] of the Office action mailed 3/19/2004) is withdrawn in view of the amendment to the claim.

[11] Claims 139-143, 164, 167-172, 177, and 204-207 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Appropriate correction is required.

[12] Claims 217 and 220-226 are objected to under 37 CFR 1.75 as being substantial duplicates of claims 144, 145, 146, 152, and 219. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 217 is

a duplicate of claim 152, claims 220 and 224 are duplicates of claim 144, claims 221 and 225 are duplicates of claim 145, claims 222 and 226 are duplicates of claim 146, and claim 223 is a duplicate of claim 219.

[13] RESPONSE TO ARGUMENT: Applicant argues "many objections are overcome by the present response" and "[o]ther objections will be overcome in conjunction with overcoming the remaining rejections applied to the same claims."

Applicants' argument is not found persuasive. The claims are improperly multiply dependent or duplicative. Appropriate correction is required.

[14] The examiner has made an earnest attempt to identify all improperly dependent or duplicate claims. In view of the numerous claims (>100), the limited time available to the examiner, and in the interest of advancing prosecution, applicant's cooperation is requested in identifying and taking appropriate action to correct any remaining improper dependency and/or duplicate claims. See particularly MPEP § 608.01(n) regarding multiple dependent claims and MPEP § 706.03(k) regarding duplicate claims.

Claim Rejections - 35 USC § 112, Second Paragraph

[15] The rejection of claims 125-127, 172, and 177 under 35 U.S.C. 112, second paragraph, (¶ [9] of the Office action mailed 3/19/2004) is withdrawn in view of the amendment to the claims.

Claim Rejections - 35 USC § 101

[16] The rejection of claims 113, 116-127, 158-162 and 218 under 35 U.S.C. 101 as being directed to non-statutory subject matter (¶ [10] of the Office action mailed 3/19/2004) is withdrawn in view of the amendment to the claims.

Claim Rejections - 35 USC § 112, First Paragraph

[17] The written description rejection of claim 133 under 35 U.S.C. 112, first paragraph, (¶ [11] of the Office action mailed 3/19/2004) is withdrawn in view of applicants' admission on the record (see p. 30 of the response filed 3/11/2005) that the "fragment" of claim 133 (and claim 136) is limited to the fragment of claim 113.

[18] The scope of enablement rejection of claim(s) 133, 136, and 162 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicants' clarifying remarks (claims 133 and 136) or upon further consideration (claim 162).

[19] The scope of enablement rejection of claim(s) 137-143, 149-151, 157-161, 163-164, 167-168, 177-180, 203, and 218 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record (¶ [12] of the Office action mailed 3/19/2004) and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue that the claims were indicated as being allowable in a previous Office action and are now rejected. Applicants argue that in providing reasoning for rejecting the claims, the examiner misstates the breadth of the claims, makes conclusory remarks regarding the working examples, overlooks certain (unidentified) teachings of the specification and the skill in the art, states there is a high level of unpredictability in the art without providing pertinent evidence, and

contradicts statements made in the obviousness rejection. According to applicants, the reasoning set forth by the examiner does not establish a prima facie enablement rejection.

The examiner maintains the position that the specification in view of the state of the art at the time of the invention fails to enable the full scope of the claimed invention.

Regarding the previous indication of allowability of the rejected claims, it is noted that, upon reconsideration of the claims, the examiner has properly withdrawn the indicated allowability. Thus, applicants' argument is moot.

Regarding the alleged misstatement of the breadth of the claims, it is noted that certain of the claims do not recite a particular function, namely claims 133 and 136. The statements regarding a lack of function were directed to these claims as the remaining claims would appear to encompass nucleic acids encoding polypeptides with a defined function. At the time of drafting the rejection, there was no indication on the record as to applicants' intended narrow scope of nucleic acids that are encompassed by claims 133 and 136. Prior to such remarks, claims 133 and 136 encompassed nucleic acids encoding polypeptides that may have any function. Thus, contrary to applicants' assertion, the breadth of claims 133 and 136 was not misstated.

Regarding the "conclusory" remarks given about the disclosed working examples, the examiner stated in a previous Office action that the specification disclosed the working examples of SEQ ID NO:1, 3, 43, 44, 46, 48, and 49. If the specification discloses additional working examples, applicants are requested to point out such working examples for the examiner's consideration. Absent evidence to the

contrary, the examiner maintains that the specification discloses only these working examples.

Regarding the assertion that the examiner has overlooked teachings of the specification and the prior art, it is unclear to the examiner as to what specific teachings have been overlooked. Applicants' cooperation is requested in specifically identifying particular teachings of the specification and/or prior art that the examiner has overlooked that would guide a skilled artisan in altering the sequences of the working examples with an expectation that these variant nucleic acids would encode polypeptides that maintain the desired activity/utility.

Regarding the assertion that no evidence pertinent to "this particular art" has been provided to support a high level of unpredictability, it is noted that the examiner has made of record the reference of Branden et al. (cited in the Office action mailed 3/19/2004), the teachings of which are undisputed by applicants. The teachings of Branden et al. are general teachings, i.e., they are not meant to be directed to any one particular protein, but to proteins in general. If the teachings of Branden et al. were specific to a particular protein, then applicants' argument may be considered valid. However, this is not the case, and the teachings of Branden et al. support the examiner's assertion that there was (and still is) a high level of unpredictability in altering a protein's encoded sequence with an expectation of maintaining the desired activity/utility. It is unclear to the examiner as to how these teachings are not pertinent to the nucleic acid/protein art. If applicants maintain that these teachings are not pertinent

to "this particular art," applicants are requested to specifically identify how the teachings of Branden et al. do not apply to "this particular art."

Regarding applicants' assertion that the instant rejection contradicts the statements made in the obviousness rejection, as noted above, the examiner indicated that certain nucleic acids were enabled by the specification (see ¶ [12] at p. 6 of the previous Office action) and made an obviousness rejection (see ¶ [13] at p. 10 of the previous Office action) on the specific nucleic acids indicated as being enabled. The rejection under 35 U.S.C. 103(a) was not directed to those nucleic acids that were asserted to be non-enabled by the specification. As such, there is no inconsistency in the scope of enablement and obviousness rejections. Although this was expressed and made clear to applicant during the interview conducted 8/3/2004, applicants nonetheless continue to make such an assertion. Regardless, in view of withdrawal of the rejection under 35 U.S.C. 103(a), applicants' argument is moot.

Addressing the reference of Branden et al. applicants argue that the cited teachings of Branden et al. are insufficient to support a prima facie enablement rejection. Applicants note the claims recite "meaningful biological function," which function can be tested using assays of the specification and prior art. Applicants argue the Office admits that "the technical steps to practice the claimed invention are enabled," but concludes that variants of the specific working examples are not enabled. According to applicants, this is not a proper conclusion under the controlling case law on the enablement requirement.

Applicants' argument is not found persuasive. Although not expressly stated, the examiner presumes, the "controlling case law" to which applicants refer is In re Wands, which summarizes the factors to be considered in determining whether undue experimentation is required as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP § 2164.01(a) states that "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others." Thus, if the rejection were based solely on a high level of unpredictability that is evidenced by Branden et al., the examiner would agree with applicants' assertion that the teachings of Branden et al. alone do not support the instant rejection. However, the examiner has not "conclude[d] that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others." Instead, the examiner has based the instant rejection on those relevant Factors of In re Wands, in accordance with MPEP § 2164.04, which states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope

of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." As noted in a previous Office action, the instant rejection is based not only on the relevant teachings of Branden et al., but on the breadth of the claims, the lack of guidance and working examples, the high level of unpredictability, and the amount of experimentation required to make the claimed nucleic acids. See particularly pp. 7-9 of the Office action mailed 3/19/2004.

The examiner acknowledges that methods of altering a nucleic acid sequence were known at the time of the invention and further acknowledges that the specification discloses an assay for detecting those nucleic acids that encode polypeptides having the desired activity/utility (pp. 205-206). However, while such methods were known in the art at the time of the invention, it was not routine in the art to screen, essentially by a trial and error process, for all nucleic acids having a substantial number of modifications, as encompassed by the instant claims.

Applicants argue that the requirements to make and use the claimed nucleic acid are the same as the requirements to make and test the claimed nucleic acid. Applicants argue that making the full scope of claimed nucleic acids requires only mutating a nucleic acid, testing its biological activity, and using the nucleic acid to promote transcription. Applicants argue there is no objective evidence that a skilled artisan could not conduct nucleic acid hybridization, identify an active encoded protein, and use it in transcription as required by the claims and further argue that, absent reason to doubt the objective truth of the specification, the disclosure must by taken as in compliance with the enablement requirement, citing In re Marzocchi.

Applicants' argument is not found persuasive. Regarding applicants' reliance on In re Marzocchi, it is noted that this case law is inapposite to the instant situation. In In re Marzocchi, the Office failed to provide objective evidence as to why all compounds encompassed by the term "polyethyleneamine" would not function as an adhesion enhancer. However, in this case, there is no dispute that the scope of claimed nucleic acids would encode polypeptides having the asserted kinase activity and the ability to promote transcription. The issue is not whether the claimed nucleic acids would encode such polypeptides. The issue is whether undue experimentation is required to make the full scope of the claimed nucleic acids. The examiner maintains that undue experimentation is required to make all nucleic acids as broadly encompassed by the claims. The claims are drawn to variant nucleic acids encoding polypeptides having a particular biological function. While it is noted that certain of the claims recite nucleic acids that are structurally related by their ability to hybridize under particular conditions, this does not include only those nucleic acids that are "naturally-occurring" and does not exclude nucleic acids produced by mutation. In this case, the specification fails to provide any specific guidance for altering the nucleic acids of SEQ ID NO:1, 3, 43, 44, 46, 48, and 49 with an expectation that these nucleic acids will encode polypeptides having the desired activity/utility. Without such guidance, one must experiment by a trial and error process, generating a vast number of variant nucleic acids to determine which of those has the desired activity/utility. The reference of Watson et al. ("Recombinant DNA," 2nd Ed., W.H. Freeman and Company, New York) teaches that the function of an enzyme is dependent upon folding of its primary amino acid sequence (p. 4, right

column). Watson et al. teach that "the specific amino acid sequence of a given enzyme is thus very important" and that "[i]f inappropriate amino acids are present, then the polypeptide chain cannot fold up to form the properly shaped catalytic cavity" (p. 4, right column). Thus, alteration of an encoded protein's sequence can alter the folding of the protein, and consequently disrupt the desired activity of a protein. As noted above, methods of altering a protein's encoded sequence were known in the art at the time of the invention. However, there was no way to know a priori those mutations that would have an undesired effect on a protein's activity. As such, appropriate guidance regarding those amino acids or regions of a polypeptide that can be altered without disrupting the desired activity/utility is necessary to prevent a skilled artisan from resorting to trial and error experimentation to create all mutants as encompassed by the claims comprising a significant number of alterations, including multiple nucleotide substitutions, additions, deletions, and insertions, which was not routine at the time of the invention. As noted in a previous Office action, Branden et al. teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). Clearly, the teachings of Branden et al. are evidence that, at the time of the invention, the effects of amino acid substitution on the function of a protein were (and still are) highly unpredictable. Further evidence is provided by the reference of Creighton ("Protein

Structure," Oxford University Press, New York), which, regarding alteration of the amino acid sequence of a protein teaches, "...without knowledge of the protein's tertiary structure, it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect" (sentence bridging pp. 185-186). Even today, the effects of altering a protein's sequence are highly unpredictable as evidenced by Witkowski et al. (Biochemistry 38:11643-11650), which teaches that altering only a single amino acid in the sequence of a polypeptide can convert the catalytic function of the polypeptide from a beta-ketoacyl synthase to a malonyl decarboxylase. In view of the high level of unpredictability as evidenced by Branden et al., the teachings of which are undisputed by applicants, and Creighton, one must, by a trial and error process, make the variants as encompassed by the claims and screen for those that have the desired activity/utility. While Creighton acknowledges that knowledge of a protein's tertiary structure can aid in providing guidance for altering a protein's sequence to maintain a desired activity/utility, there is no evidence of record that the tertiary structure of either subunit of P-TEFb was known in the art at the time of the invention.

At least for the reasons of record and the reasons stated above, the specification in view of the prior art fails to enable the full scope of the claims without the need for undue experimentation.

Claim Rejections - 35 USC § 103

[20] The rejection of claim(s) 110-111, 113, 116-129, 133-137, 147-149, 152, 157-161, 164, 167-169, 178-181, 183, 186, 195-201, 203-208, 211-213, 215-218 under 35 U.S.C. 103(a) as being unpatentable over Marshall et al. in view of Matsudaira, Wozney, and Ausubel et al. is withdrawn in view of further consideration of the rejection. As noted in the interview summary of the telephonic interview conducted on 8/3/2004, upon further discussion with Office practice specialists, it was decided that the rejection should be withdrawn.

Conclusion

[21] Status of the claims:

Claims 110-113, 116-164, 167-172, 174-181, 184, 186-189, 191-193, 195-208, and 211-226 are pending.

Claims 137-143, 149-151, 157-161, 163-164, 167-168, 177-180, 203, and 218 are rejected.

Claims 169-172, 174-176, 204-207, 217, and 220-226 are objected to for the reasons stated above.

Claims 144-146 and 162 are objected to as being dependent upon a rejected/objected base claim, but would be appear to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 110-113, 116-136, 147-148, 152-156, 181, 184, 186-189, 191-193, 195-202, 208, 211-216, and 219 appear to be in condition for allowance.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (571) 273-8300. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER